

### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT).

(51) International Patent Classification 6:		(11) Internati nal Publication Number:	WO 98/53801
A61K 9/127, 31/70, 38/00, C07H 21/00, C07K 1/00, 1/13, 2/00, C12N 5/00, C12O	A1	(43) Internati nal Publication Date:	3 December 1998 (03.12.98)

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Published

With international search report.

(54) Title: CONJUGATED PEPTIDE NUCLEIC ACIDS HAVING ENHANCED CELLULAR UPTAKE

(57) Abstract

Peptide nucleic acids conjugated to lipophilic groups and incorporated into liposomes exhibit enhanced cellular uptake and distribution. Cellular uptake and distribution of peptide nucleic acids also increases with the introduction of an amino acid side chain into the backbone of peptide nucleic acids. Methods of modulating cellular uptake and methods for treating animals are provided. The peptide nucleic acids of the invention comprise naturally-occurring nucleobases and non-naturally-occurring nucleobases attached to a polyamide backbone.

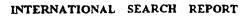




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International application No.

PCT/US98/10804

A. CLASSIFICATION OF SUBJECT MATTER				
IPC(6) :Please See Extra Sheet. US CL :Please See Extra Sheet.				
According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELD	OS SEARCHED			
Minimum do	cumentation searched (classification system followed	by classification symbols)		
U.S. : 42	24/450; 435/6, 325, 375; 514/2, 44; 530/300, 333; 53	6/23.1, 24.3, 24.5, 25.3, 25.32; 568/818		
Documentation	on searched other than minimum documentation to the	extent that such documents are included	in the fields searched	
	ats base consulted during the international search (nar Extra Sheet.	ne of data base and, where practicable,	search terms used)	
C. DOC	UMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to elaim No.	
A	US 5,539,082 A (NIELSEN et al.) 23 to column 11, line 9.	July 1996, column 2, line 65	1-52	
A	WO 97/14026 A2 (LANSDORP) 17 April 1997, page 6, lines 18-24, page 8, line 33 to page 9, line 6, page 10, lines 27-35.			
A Amine Reactive Fluorescent Probes: Offering a selection of succinimidyl esters, isothiocyanates and sulfonyl halides. Pierce ImmunoTechnology Catalog and Handbook. 1992, page b. 65.				
Further documents are listed in the continuation of Box C. See patent family annex.				
<b>i</b> .	perial categories of cited documents:	"I" later document published after the int		
"A" document defining the general state of the art which is not considered to be of particular salevance date and not in conflict with the application but cited to understand the principle or theory underlying the invention				
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special reason (as specified)  "Y"  document of particular relevance; the claimed invention cannot be considered to involve an inventive stap when the document of combined with one or more other such document, such combination			s step when the document is the documents, such combination	
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1	e actual completion of the international search UST 1998	Date of mailing of the international se		
Commissi Box PCT	mailing address of the ISA/US oner of Patents and Trademarks	Authorized officer THOMAS G. LARSON, PH.D.		
Washington, D.C. 20231 Facsimile No. (703) 305-3230		Telephone No. (703) 308-0196		

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International application No. PCT/US98/10804

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6): A61K 9/127, 31/70, 38/00; C07H 21/00; C07K 1/00, 1/13, 2/00; C12N 5/00; C12Q 1/68

A. CLASSIFICATION OF SUBJECT MATTER:

US CL : 424/450; 435/325, 375; 514/2, 44; 530/300, 333; 536/23.1, 25.3, 25.32

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN (BIOSIS, CAPLUS, CJACS, INPADOC, MEDLINE, REGISTRY, WPIDS)

Search Terms: peptide nucleic acid, PNA, adamantoyl, fluoroscein, lysine, lipophilic, uptake, label, conjugate, Nielsen, Peter E.

# PATENT COOPERATION TREATY

## **PCT**

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference		San National of Taxable of Languing		
ISIS-3045 FOR FURTHER AC		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)		
International application No. International filing date		nonth/year) Priority date (day/month/year)		
PCT/US98/10804 28 MAY 1998		28 MAY 1997		
International Patent Classification (IPC) Please See Supplemental Sheet.	or national classification and IP	· · · · · · · · · · · · · · · · · · ·		
Applicant NIELSEN, PETER E.				
Examining Authority and is	transmitted to the applicant a	been prepared by this International Preliminary according to Article 36.		
2. This REPORT consists of a	total of sheets.			
been amended and are the (see Rule 70.16 and Sec	ne basis for this report and/or she tion 607 of the Administrative	ets of the description, claims and/or drawings which have eets containing rectifications made before this Authority. Instructions under the PCT).		
These annexes consist of a to	otal of sheets.			
3. This report contains indication	ns relating to the following it	ems:		
I X Basis of the repo	rt			
II Priority				
III Non-establishme	at of report with regard to no	velty, inventive step or industrial applicability		
IV Lack of unity of	invention			
V X Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement				
VI Certain documents cited				
VII Certain defects in the international application				
VIII Certain observations on the international application				
Date of submission of the demand	of completion of this report			
04 DECEMBER 1998	04	FEBRUARY 1999		
Name and mailing address of the IPEA/		orized officer		
Commissioner of Patents and Tradent Box PCT		HOMAS G. LARSON, PH.D.		
Washington, D.C. 20231  Facsimile No. (703) 305-3230		hone No. (703) 308-0196		



International application No.	
PCT/US98/10804	

the report			
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the description,	pages 1-47	_ , as originally filed.	
	pages NONE	_ , filed with the demand.	
	pages NONE	, filed with the letter of	
	pages	, filed with the letter of	
the claims,	Nos. <u>1-52</u>	, as originally filed.	
	Nos. NONE	, as amended under Article 19.	
	Nos. NONE	, filed with the demand.	
	Nos. NONE	, filed with the letter of	
	Nos	, filed with the letter of	
the drawings,	sheets/fig 1	, as originally filed.	
	sheets <del>/fig</del> NONE	, filed with the demand.	
	sheets/ <del>fig</del> NONE	, filed with the letter of	
	sheets <del>/fig</del>	, filed with the letter of	
the description, the claims, the drawings, s report has been es to beyond the disclo	pages NONE  Nos. NONE  sheets/fig NONE  stablished as if (some of) stars as filed, as indicated	the amendments had not been made, since they have been considered	
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	the description, the description, the drawings, the description, the description, the description, the description, the drawings, sreport has been es	the international application as originally filed the international application as originally filed the international application as original the description, pages 1-47  pages NONE  pages NONE  pages NONE  pages NONE  NOS. NONE  The drawings, sheets/fig NONE  sheets/fig NONE  the description, pages NONE  the claims, Nos. NONE  the drawings, sheets/fig NONE  the drawings, sheets/fig NONE  the drawings, sheets/fig NONE  the drawings, sheets/fig NONE  sreport has been established as if (some of)	has been drawn on the basis of (Substitute sheets which have been furnished to the rectiving Office in response to an invitation to 14 are inferred to in this report as "originally filed." and are not annexed to the report since they do not contain amendments):  the international application as originally filed.  the description, pages 1-47, as originally filed.  pages NONE, filed with the demand.  pages NONE, filed with the letter of, as originally filed.  Nos. NONE, as originally filed.  Nos. NONE, as originally filed.  Nos. NONE, filed with the letter of, nos. NONE, filed with the letter of, filed with the letter of, nos. NONE, filed with the letter of, filed with the letter of, filed with the demand.  sheets/fig NONE, filed with the letter of, filed with the letter of

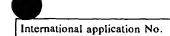


#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

# International application No. PCT/US98/10804

STATEMENT			
Novelty (N)	Claims	1-52	 YE
	Claims	NONE	 NO
Inventive Step (1S)	Claims	1-52	 YE
	Claims		
			· <del>-</del> :
Industrial Applicability (1A)	Claims	1-52	 YE
	Claims	NONE	 NO
NEW CITATIONS NONE			
	·		





PCT/US98/10804

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:** 

The International Patent Classification (IPC) and/or the National classification are as listed below: IPC(6): A61K 9/127, 31/70, 38/00; C07H 21/00; C07K 1/00, 1/13, 2/00; C12N 5/00; C12Q 1/68 and US CI.: 424/450; 435/325, 375; 514/2, 44; 530/300, 333; 536/23.1, 25.3, 25.32

### ATENT COOPERATION TRE Y

NOTIFICATION OF ELECTION (PCT Rule 61.2)  Date of mailing (day/month/year) 08 January 1999 (08.01.99)  International application No. PCT/US98/10804  International filing date (day/month/year) 28 May 1998 (28.05.98)  Applicant NIELSEN, Peter, E. et al  1. The designated Office is hereby notified of its election made:  \[ \begin{array}{c c c c c c c c c c c c c c c c c c c		From the INTERNATIONAL BUREAU		
Office (Box PCT) Crystal Plaza 2 Washington, DC 20231 ÉTATS-UNIS D'AMÉRIQUE  in its capacity as elected Office    National application No.   PCT/US98/10804   International filling date (day/month/year)   28 May 1998 (28.05.98)   28 May 1997 (28.05.97)    Applicant   NIELSEN, Peter, E. et al	PCT	To:		
International application No. PCT/US98/10804  International filing date (day/month/year) 28 May 1998 (28.05.98)  Applicant NIELSEN, Peter, E. et al  1. The designated Office is hereby notified of its election made:  X in the demand filed with the International Preliminary Examining Authority on:  04 December 1998 (04.12.98)  in a notice effecting later election filed with the International Bureau on:  2. The election X was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under		Office (Box PCT) Crystal Plaza 2 Washington, DC 20231		
International filing date (day/month/year) 28 May 1998 (28.05.98)  Applicant NIELSEN, Peter, E. et al  1. The designated Office is hereby notified of its election made:  X in the demand filed with the International Preliminary Examining Authority on:  04 December 1998 (04.12.98)  in a notice effecting later election filed with the International Bureau on:		in its capacity as elected Office		
28 May 1998 (28.05.98)  28 May 1997 (28.05.97)  Applicant  NIELSEN, Peter, E. et al  1. The designated Office is hereby notified of its election made:  X in the demand filed with the International Preliminary Examining Authority on:  04 December 1998 (04.12.98)  in a notice effecting later election filed with the International Bureau on:  2. The election X was  was not  made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under		7.		
NIELSEN, Peter, E. et al  1. The designated Office is hereby notified of its election made:    X   in the demand filed with the International Preliminary Examining Authority on:   04   December 1998 (04.12.98)     in a notice effecting later election filed with the International Bureau on:   2. The election   X   was   was not   was not   was not   was not   was not   was priority date or, where Rule 32 applies, within the time limit under				
1. The designated Office is hereby notified of its election made:    X   in the demand filed with the International Preliminary Examining Authority on:   04   December 1998 (04.12.98)   in a notice effecting later election filed with the International Bureau on:   2. The election   X   was   was not   was not   was not   was not   was not   was not   was priority date or, where Rule 32 applies, within the time limit under				
in the demand filed with the International Preliminary Examining Authority on:  O4 December 1998 (04.12.98)  in a notice effecting later election filed with the International Bureau on:  7. The election X was was not  made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under	NIELSEN, Peter, E. et al			
	1. The designated Office is hereby notified of its election made:    X   in the demand filed with the International Preliminary Examining Authority on:   04   December 1998 (04.12.98)   in a notice effecting later election filed with the International Bureau on:   2. The election   X   was   was not   was not   was not   was not   was from the priority date or, where Rule 32 applies, within the time limit under			

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